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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NEW YORK, NY 10110

EXAMINER

TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 07/29/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/390,851

Applicant(s)

PEDERSEN ET AL.

Examiner

My-Chau T. Tran

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28-55 is/are pending in the application.
- 4a) Of the above claim(s), 34, 40-47 and 54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 28-33, 35-39, 48-53, and 55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

Note: The examiner for your application in the PTO has changed. However, the Group and/or Art Unit location of your application in the PTO is remained the same, which is Group Art Unit 1639.

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. Applicant's amendment filed 5/20/03 in Paper No. 25 is acknowledged and entered.
3. Claims 28-55 are pending.

Election/Restrictions

4. Applicant's election without traverse of Group I (Claims 28-34 (in part), 35-39, 48 (in part), 49, and 50-55 (in part) in Paper No. 18 is acknowledged.
5. Claims 40-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 18.

Note: There were four designated groups in the restrictions in Paper No. 18 and the groups are as follows:

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- a. Group II: Claims 28-34 (in part), **40-43**, 48 (in part), and 50-55 (in part).
 - b. Group III: Claims 28-34 (in part), **44-45**, 48 (in part), and 50-55 (in part).
 - c. Group IV: Claims 28-34 (in part), **46-47**, 48 (in part), and 50-55 (in part).
6. Applicant's election without traverse in Paper No. 18 is acknowledged of the following species:
- a. Species of "catalytic activity of interest": protease activity.
 - b. Species of "biological amplifiable unit": a phage.
 - c. Species of substrate: protease.
 - d. Species of "selecting in claim 1 (ii)": the selection step of immobilizing the product molecule. *Note:* Since claim 1 was cancel in Paper No. 17, the elected species is interpreted as step (e) of claim 28.
 - e. Species of "attachment of catalyst to substrate": covalent attachment.
 - f. Species of "flexible linker in claim 31": polyethylene glycol (PEG).
 - g. Species of "a carrier system in claim 32": phage-peptide carrier system.
7. Claims 34 and 54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 18.

Terminal Disclaimer

8. The terminal disclaimer filed on 5/20/03 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of application no. 09/395,017 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 5/20/03 is sufficient to overcome the nonstatutory double patenting rejection over copending Application No. 09/395,017.

9. Applicant's arguments with respect to the rejection under 35 USC 112, first paragraph, (scope of enablement) for Claims 28-39 and 48-55 have been considered but are moot in view of the new ground(s) of rejection.

10. Claims 28-33, 35-39, 48-53, and 55 are treated on the merit in this Office Action.

New Rejections

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 28-33, 35-39, 48-53, and 55 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

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application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims encompass a broad genus of starting materials (catalysts), and products. For example, claim 28 outlines steps for (a) “providing a library of catalysts comprising at least two different units wherein each unit comprises a catalyst attached to at least one substrate, each unit having the structure catalyst-substrate, catalyst-flexible linker-substrate (claim 31), catalyst-carrier system-substrate (claim 32), and/or catalyst-flexible linker- carrier system-substrate (claim 33), wherein said catalyst is attached to said at least one substrate in a manner that allows a catalytic reaction to occur between said catalyst and said at least one substrate”, (b) “providing conditions suitable for said catalyst to catalyze the reaction of said at least one substrate to form one or more products, wherein at least one product of said catalytic reaction remains attached to said catalyst”, (c) “providing at least one reagent or condition which converts said at least one product to at least one substrate as to regenerate said catalyst-substrate units”, and (d) “selecting said catalyst with the desired catalytic activity.”

The scope of this catalyst library includes an infinite number of catalysts with an infinite number of structural variants (i.e., library members and core structures that are in claims 31-33) wherein no distinguishing structural attributes are provided for the library members. For example in a single core structure of catalyst-flexible linker-substrate (C-F-S), the structure would encompass an infinite numbers of structural variants such as C-F-S, C-F-S-C, C-S-F-C, C-F-S₂, C-F-S₂-C, C-S₂-F-C, C₂-F-S, C₂-F-S-C₂, C₂-S-F-C₂, C₂-F-S₂, or C₂-F-S₂-C₂, etc., and the flexible linker (F) itself would encompass an infinite numbers of structural variants such as metal, organometallic, or polymers. Since the library of catalysts comprising at least two

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different units, the catalyst library would encompass a pool of catalyst with different core structures (e.g. mixture different combination of core structures), or a mixture of structural variants within a single core structure. Additionally, the interaction (e.g. functionality) of the catalyst with the substrate, transition state, and/or product of a desired reaction would depend on the type of functional group(s) on the catalyst. Therefore, the limitation “wherein said catalyst is attached to said at least one substrate in a manner that allows a catalytic reaction to occur between said catalyst and said at least one substrate” would not provide any guidance as to the structure of the catalyst. The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the catalytic members of the catalyst library (e.g. includes such catalyst as metal, organometallic compounds and enzymes). Although the specification discloses many possible catalysts that “might” be used to form the catalysts libraries (see Specification, pages 7-9 and 24-25), the specification and claims do not provide any guidance as to what structural features all of these catalysts would share.

Consequently, it is not possible to determine *a priori* which compounds the “catalyst” libraries would encompass or the product of the catalytic reaction because there is no common structural attributes that can link together all of these potential catalysts in library i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* all the different types of compounds that should be included in this genus from the few examples provide by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails

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to describe the common attributes or characteristics that identify all of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing examples like Snase, Rnase A, and DNA polymerase Klenow fragment catalysts that are known in the literature (see examples 1-9) is insufficient to teach the entire genus (e.g. catalyst such as metal, and organometallic compounds). Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

The scope of the method step (i.e. “providing at least one reagent or condition which converts said at least one product to at least one substrate as to regenerate said catalyst-substrate units”) includes an infinite number of catalyst-substrate that could be regenerated. Since there are an infinite number of catalysts to be use as the starting material then it is unknown as to which catalytic reaction is reversible to produce the regenerated “catalyst-substrate”. The specification and claims do not provide place any limit as to any type of catalyst that would have a reversible catalytic reaction (e.g. to convert the product to the substrate). Although the specification discloses as to how to search for reagent that would covert the product back to the substrate (see specification pg. 21-24), the specification and claims do not provide any guidance as to which catalyst that can have a reversible catalytic reaction.

Consequently, it is not possible to determine *a priori* which compounds the “catalyst” libraries would have a reversible catalytic reaction from all of these potential catalysts in library i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* all the reversible catalytic reaction that should be included in this genus from the few examples provide by applicants.

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The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify all of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing examples like ATP-dependent isomerization, or RNA polymerization (see pg. 22-23) is insufficient to teach the entire genus (e.g. lyases, oxidoreductases, or cleavages). Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

Finally, applicant is directed to the University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the claimed invention contains not identifying characteristics regarding the library of product, guidance for the method of "selecting the catalyst" of interest from a regenerated library of catalyst, and guidance for method of regenerating a library of catalyst when the starting material is unknown. The specification disclosure clearly does not

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teach scope of library of catalyst and the method for regenerating library of catalyst-substrate of the presently claimed invention.

13. Claims 28-33, 35-39, 48-53, and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims briefly recite a method for identifying a catalyst of interest from a library of catalysts. For example, claim 28 outlines steps for (a) “providing a library of catalysts comprising at least two different units wherein each unit comprises a catalyst attached to at least one substrate, each unit having the structure catalyst-substrate, catalyst-flexible linker-substrate (claim 31), catalyst-carrier system-substrate (claim 32), and/or catalyst-flexible linker-carrier system-substrate (claim 33), wherein said catalyst is attached to said at least one substrate in a manner that allows a catalytic reaction to occur between said catalyst and said at least one substrate”, (b) “providing conditions suitable for said catalyst to catalyze the reaction of said at least one substrate to form one or more products, wherein at least one product of said catalytic reaction remains attached to said catalyst”, (c) “providing at least one reagent or condition which converts said at least one product to at least one substrate as to regenerate said catalyst-substrate units”, and (d) “selecting said catalyst with the desired catalytic activity.”

The specification disclosures teach the individuals steps by not the combinations of the individual steps for the method for identifying a catalyst of interest from a library of catalysts. The specification discloses many possible catalysts that “might” be used to form the catalysts

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libraries (see Specification, pages 7-9 and 24-25) and how to search for reagent that would convert the product back to the substrate (see specification pg. 21-24). The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the catalytic members of the catalyst library (e.g. includes such catalyst as metal, organometallic compounds and enzymes). The specification and claims do not provide place any limit as to any type of catalyst that would have a reversible catalytic reaction (e.g. to convert the product to the substrate). The specification fails to teach the method for identifying a catalyst of interest from a library of catalysts wherein the first step is providing a "mixture" of catalyst (library of catalyst), providing a condition that the catalyst convert the substrate to a product, providing a condition that convert the product back to the substrate, and then selecting the catalyst with the desired catalytic activity of interest.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (U.S.P.Q. 2d 1400: CAFC 1988) which include: quantity of experimentation necessary; the amount of direction or guidance presented; the presence or absence of working examples; the nature of the invention; the state of the prior art; the predictability of the art; and the breadth of the claims.

A number of factors would prevent one of ordinary skill in the art from practicing (the method for identifying a catalyst of interest from a library of catalysts) the invention without undue experimentation, which are summarized as follows:

- a. The specification fails to give adequate direction and guidance to perform the method for identifying a catalyst of interest from a library of catalysts with the following method steps: providing a "mixture" of catalyst (library of catalyst), providing a condition that the catalyst

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convert the substrate to a product, providing a condition that convert the product back to the substrate, and then selecting the catalyst with the desired catalytic activity of interest. The first step begins with a mixture of catalyst with “unknown” core structure. For example, the library of catalyst comprises of catalyst such C_a , C_b , C_c , substrate S_a , S_b , S_c , and a structure of C-S. This library would have a possible combination of C_a-S_a , C_a-S_b , C_a-S_c , C_b-S_a , C_b-S_b , C_b-S_c , C_c-S_a , C_c-S_b , C_c-S_c , etc. The specification does not provide any guidance as to the type of condition is “use” in which the catalyst convert the substrate into a product in a library of catalyst and the type of product is being form (e.g. C_a-P_a , C_a-P_b , C_a-P_c , C_b-P_a , C_b-P_b , C_b-P_c , C_c-P_a , C_c-P_b , C_c-P_c , etc.). Each catalyst would require a different “condition” in order to form a product.

Additionally, cross-reaction can occurs within a mixture of catalyst (e.g. instead of C_a reacting with S_a the catalyst C_b of the C_b-S_a can react with S_a). The specification does not provide any guidance as to the type of condition is “use” in which the product is converted back to the substrate and which product is being converted in the library of catalyst. Each product would require a different “condition” in order to convert the product back to the substrate.

Additionally, type of substrate being produce from the reaction is unknown because is the substrate the same as the original substrate or different. From this library the catalyst with the desired catalytic activity of interest is selected. The specification does not provide any guidance as to selecting the catalyst with the desired catalytic activity of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalyst. Therefore, the specification does not teach the present invention.

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c. The breath of the claims is open-ended regarding the type of catalyst; the type product produce in the forward reaction; the type of substrate produce in the reverse reaction; condition for the forward; and condition for the reverse.

d. The state of the prior art at the time the invention was made is such that each type of catalyst requires different reaction conditions (e.g. catalytic activity) and produces different product. In general the synthesis of libraries of catalyst do not have standard method and testing for their reactivities are known to be difficult.

e. The art is inherently unpredictable because each type of catalyst has different catalytic activity and to select the catalyst with the desired catalytic activity of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalyst.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 28-33, 35-39, 48-53, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Clarification is need as to the distinction is being consider as “different” (e.g. type of catalyst, type of substrate, addition of a “linker” or ‘carrier system’) in the term “different unit” of claim 28.

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b) Step (e) of claim 28 is vague and indefinite because it is unclear as to the catalyst being selected when it is unclear as to which of the "two different unit" (e.g. catalyst-substrate) is being regenerated.

c) The term "conditions suitable" of claim 28 is a relative term, which renders the claim indefinite. The term "conditions suitable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

d) It is unclear in the step (c) of claim 28 as to the means and bounds of the reagent or condition is being considered to convert the "product" of a catalytic reaction to the "substrate" of the catalytic reaction (e.g. the same reagent or condition used to catalyze the substrate to the product).

e) Clarification is needed as to the link between the step of converting the product back to the substrate and the step of selecting the catalyst by immobilizing the product in claim 50.

16. Claims 28-33, 35-39, 48-53, and 55 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The link between the step of converting the product back to the substrate and the step of selecting the catalyst (e.g. the product (regenerate catalyst-substrate) is the same as the starting material (catalyst-substrate)).

17. Claims 50-53 and 55 recite the limitation "selecting step" in line 1. There is insufficient antecedent basis for this limitation in the claim 29.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct
July 28, 2003


PADMASHRI PONNALURI
PRIMARY EXAMINER